REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-4 and 9-27 were pending in this application when last examined.

Claims 1-4 and 9 were examined on the merits and stand rejected.

Claims 10-27 were withdrawn as non-elected subject matter. The right to rejoinder is hereby reserved.

Claim 1 is cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a Continuation or Divisional Application on any cancelled subject matter.

Claims 2-4 and 9 are amended to clarify the claimed invention and to correct informalities in view of the cancellation of claim 1.

Claim 29 is newly added. Support can be found in the claims as filed.

No new matter has been added.

II. CLAIM OBJECTION

On pages 4-5 of the Office Action, claims 1 and 2 were objected to for the noted informalities. Claim 1 is cancelled without prejudice and therefore these objections are overcome. Furthermore, with regard to new claim 29, it is noted that AlcR is not an abbreviation but is instead a designation of a protein. Furthermore, as indicated on page 6 of the Office Action, the *Aspergillus nidulans* AlcR protein can easily be found in databases and is unequivocally defined, showing that there is no need for further explanation of AlcR.

In regard to claim 2, these rejections are overcome for reasons which are self-evident.

III. ENABLEMENT REJECTION

On pages 5-9 of the Office Action, claims 1-4 and 9 were rejected under 35 U.S.C. § 112, first paragraph, for failing to meet the enablement requirement. Applicants respectfully traverse this rejection as applied to the amended claims.

On page 6, it is noted that the Examiner indicates that the specification is enabling for an isolated mammalian cell comprising:

(a) a nucleic acid encoding a promoter operatively linked to a nucleic acid sequence encoding an acetaldehyde-responsive transcription factor AlcR protein, and (b) a nucleic acid comprising a promoter said promoter operatively linked to an *A. nidulans* AlcR-specific PalcA operator sequence obtained by amplifying said operator site PAlcA sequence from a PalcA containing vector with oligonucleotides of SEQ ID No.1 and SEQ ID No.2.

Without acquiescence to the correctness of the Examiner's position, claim 29, the only independent claim under examination on the merits, has been amended to that which is considered enabled by the Examiner. Thus, this rejection is overcome and should be withdrawn.

IV. ANTICIPATION/OBVIOUSNESS REJECTION

On pages 9-13 of the Office Action, claims 1, 2, 4 and 9 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Caddick et al. (U.S. Patent No. 6,605,754) in view of White (Internet article November 11, 1999). Further, on pages 13-15, claims 1 and 3 were rejected under 35 U.S.C. 10 § 103(a) as being obvious over Caddick et al., in view of White and further in view of Flipphi et al. Applicants respectfully traverse these rejections as applied to the amended claims.

In particular, Applicants note that the cited references fail to teach a reasonable expectation of success to arrive at the claimed invention. In particular, a person of skill in the art would understand that the suggestion in White is defective as isolated mammalian cells are not expected to metabolize ethanol to acetylaldehyde. Thus, a person of skill in the art would not be motivated to combine these references and allegedly arrive at the claimed invention. In particular, Applicants note the following:

Caddick et al. disclose a chemically-inducible plant gene expression cassette comprising a first promoter, e.g. the alcA gene promoter (the alcA gene encodes alcohol dehydrogenase I) operatively linked to a regulator sequence which encodes a regulator protein, e.g. the AlcR regulator protein (the responsive transcription factor), whereby said alcR gene product is induced by an effective exogenous inducer, i.e. by the protein/alcohol or proteine/ketone combination.

However, the invention as now claimed is directed to a mammalian cell comprising a nucleic acid encoding the A. nidulans AlcR protein and a promoter operatively linked to P_{alcA}

operator specific for binding the AlcR protein. Significantly, in the claimed invention, the formation of the AlcR protein is dissected from the alcohol dehydrogenase.

White suggests regulating luciferase expression in mammalian cells in response to ethanol by transfection of AlcR fused to a transcriptional activator together with a luciferase expression unit driven by an alcA-derived promoter. However, this PhD study project is defective, and the proposed system has never been realized. The proposed system is not functional since ethanol is not a direct inducer of the AlcR system and would instead require metabolization into acetaldehyde to be induction effective. Such metabolization does not occur in mammalian cell culture.

Although it is known that in liver and brain cells ethanol is metabolized to acetaldehyde, an isolated mammalian cell comprising exogenous nucleic acid is a cell having undergone substantial manipulation, and is clearly different from primary brain and liver cells. Attached document (Clemens et al., Archives of Biochemistry and Biophysics 321, 311-318, 1995; **Attachment A**) shows that cultured hepatocytes lose their ability to metabolize ethanol to acetaldehyde. Eysseric et al. (Alcoholism: Clinical and Experimental Research 21, 1018-1023, 1997, of record) demonstrates production of acetaldehyde by astrocytic *primary* cells, not by astrocytes containing exogenous nucleic acid.

Thus, these two documents indicate that a skilled person in the art would not combine the teaching of Caddick et al. and White because isolated mammalian cells containing exogenous nucleic acid are not expected to metabolize ethanol to acetaldehyde.

Furthermore, Applicants note that they do not have to prove that ethanol is never metabolized to acetaldehyde in mammalian cells. Applicants merely have to show that the skilled person in the art would not be motivated to combine the teachings of Caddick et al. and White to arrive at the instantly claimed invention. Thus, Applicants note that a skilled person would understand that the White suggestion is pure speculation since isolated mammalian cells comprising exogenous nucleic acid are not expected to metabolize ethanol to acetaldehyde.

Applicants further note that the Examiner indicates that "the use of prokaryotic transcriptional regulatory elements for controlled expression of cloned genes in mammalian cells and animals was well known in the art", citing Weber, Nucleic Acid Res. 2003, of record. However, the Examiner overlooks that use of A. nidulans regulatory elements is not trivial.

A. nidulans AlcR is not a prokaryotic transcription regulator, but a eukaryotic regulator derived from fungi.

Flipphi does not add any further aspect to Caddick and White. Caddick in view of White and in view of Flipphi does not suggest introducing nucleic acid coding for the A. nidulans AlcR protein and a promoter operatively linked to P_{alcA} operator sequences into a mammalian cell by amplifying a P_{alcA} operator sequence from a vector comprising said P_{alcA} operator sequence with oligonucleotides of SEQ ID NO:1 and SEQ ID NO:2.

Thus, for the above-noted reasons, this rejection is untenable and should be withdrawn.

V. INDEFINITENESS REJECTION

On pages 15-16 of the Office Action, claims 1-4 and 9 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is overcome, as applied to new claim 29 and the claims dependent thereon for reasons which are self-evident.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Martin FUSSENEGGER et al.

By /William R. Schmidt, II/

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September 30, 2009